UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,477	01/23/2002	F.C. Thomas Allnutt	031676.0208	9546

21967 7590 11/21/2005

HUNTON & WILLIAMS LLP
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,477	ALLNUTT ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *14-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 9/7/2005 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claim 1-13 are under examination.
2. Claim 14-20 are withdrawn from further consideration.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claim 1-2, 4-8, 10-11 are rejected under 35 USC 103(a) as being unpatentable over Xu et al..

Xu et al. disclose a method of nervous ligand specificity binding protein, i.e. brain lipid-binding protein (BLBP). Xu et al. teach contacting the DHA samples with the BLBP protein (See page 24712, left column, Methods and Materials). In particular, DHA possesses higher affinity than those fatty acids (See Table I). Xu et al. teach detecting the DHA-protein (BLBP) complex (See See page 24712, left column, Methods and Materials). Although Xu et al. reference does not explicitly teach using BLBP to measure an undetermined amount of DHA, one artisan in the field in view of the Xu's report would have used the teaching as the method of detecting the presence of DHA in a biological sample. The suggestions and motivations are outlined below:

First of all, Xu et al. disclose the specificity of the BLBP to a particular target fatty acid, namely DHA having at least 20-fold higher affinity than other fatty acids (See Table I for the Kd values; and page 24717, right column, third paragraph). Second, Xu et al. disclose that DHA is a ligand for BLBP in a physiological condition, e.g. blood, urine or tissue. Lastly, Xu et al. conclude that the requirement of DHA is essential for the nervous development in vivo (page 24711, right column, second paragraph). Taken together, one ordinary skill in the art would have been motivated to use the BLBP to detect DHA as taught by Xu et al., in a physiological sample because the important role of DHA in the nervous development, the ligand relationship of DHA in the physiological condition, and the known high specificity BLBP/DHA.

With respect to claim 5, Xu et al. label fatty acid, e.g. H^3, as a detecting means to measure the binding between the fatty acid and BLBP protein (See Figure 2 and 3 and Table 1).

With respect to claim 6, Xu et al. found out that there is a 20-fold increase in affinity of BLBP for DHA compared to OA or AA (See Table I for the Kd values; and page 24717, right column, third paragraph).

With respect to claim 8, Xu et al. teach using a recombinant BLBP immobilized in a Lipidex 1000 column for fatty acid binding assay (See Methods and Materials).

With respect to claim claims 10-11, Xu et al reference has been discussed but is silent in using biological samples in the analysis. However, Xu et al. review the role of BLBP in the developing central nervous system, including cell differentiation, signal transduction, and regulatory upregulation (See Introduction). Xu et al. also disclose the DHA molecule, biological cellular membrane lipid, has a high specificity and affinity for the BLBP. Most importantly, Xu et al. also report that DHA is a physiological ligand for BLBP. Therefore, it would have been obvious to one skilled in the art at the time when invention was made to apply the method of binding between BLBP and DHA in a biological sample, such as neural tissues or blood, with reasonable expectation of success because the target ligand DHA for BHA is known, and understanding the development processes is of great interest in research field, and biological sample preparation involves merely routine practice in the art.

4. Claims 3 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al. in view of Ullman et al. (US 6326159).

Xu et al. reference has been discussed but is silent in using a protein, i.e. antibody to detect the DHA-BLBP complex or immobilized protein for detection.

Ullman et al. review a method of producing an antibody recognizing a complex formed by a target ligand bound with ligand binding partner protein and immobilized protein on a solid support is commonly used in the art (Col. 5, line 30-45; Abstract; Example 8). Ullman et al. indicate that using a second antibody specifically for the complex of ligand with ligand protein can enhance specificity of binding results (See Col. 17, line 45-60). The technique of making the antibody involves routine skilled in the art. Supra.

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to have provided Xu et al. with the antibody specific for recognizing the complex of the BLBP and DHA for enhance specificity.

5. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al. in view of Adams et al. (US 5447957).

Xu et al. reference has been discussed but is silent in teaching using hydrolyzing agent to release DHA from lipids for analysis.

Adams et al. teach using KOH, a non-enzymatic agent, to release fatty acid from lipid complex, for identification and quantitation (Col. 28, line 1-10). Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided Xu et al. with the KOH agent to release the target DHA from the lipid complex of the samples for better purity and detection efficiency.

Response to Applicant's Arguments

Xu's reference

With respect to claim 1-2, and 4-8, applicant argues that Xu et al. reference teaches determining whether and to what degree DHA (i.e. using known amounts) would bind to BLBP. Xu et al. did not detect the presence of DHA because DHA in Xu's assay was already known at a predetermined concentration (See Remarks, page 4, II).

Applicant's arguments have been considered but are not persuasive.

As indicated in this Office Action, examiner acknowledged that the experimental results of Xu et al. reference are for the binding affinity of BLBP and DHA. Nevertheless

examiner has established prima facie obviousness rejection in view of the suggestions and motivation of Xu et al. reference to one artisan in the art to detect DHA in a biological sample.

With respect to claim 10-11, applicant argues that (1) one ordinary skill in the art would not be motivated to use biological samples in Xu's study since Xu et al. is the binding affinity study, even if one considered doing so, one would not have a reasonable expectation of success because Xu's reference uses pure BLBP for binding affinity study; (2) Xu's reference teaches using radiolabeled fatty acid for detection, therefore one would not have reasonable expectation of success, under normal circumstance, to detect a non-radiolabeld biological sample and (3) one would not perform the binding affinity experiment of Xu if it were already known that a ligand for BLBP is DHA because the experiment would be moot.

Applicant's arguments have been considered but are not persuasive.

As previously discussed, examiner has established prima facie obviousness rejection in this Office Action providing motivation and suggestion to apply Xu's reference to detect sample containing DHA. With respect to radiolabled assay, one ordinary skill in the art would have using immunoassay, e.g. antibody-recognition complex, to detect target complex. Using alternative detection means, such as non-radiolabeled immunoassay, would be less burden, e.g. radio-contamination, and would merely involves routine practice in the art. Finally, one artisan in the field would not simply "repeat" what Xu's experiments, i.e. binding affinity study, rather in view of the discussion and suggestion of Xu's reference, one would have been motivated to use teachings of Xu et al. to detect biological sample containing DHA for nervous development study.

Ulman et al. reference

With respect to claim 3 and 9, applicant argues that there is no suggestion or motivation to combine Xu's teaching with Ulman's teachings, furthermore assuming both references are combined, it would not produce the recited invention because Xu's reference is determining binding affinity, not a detection assay (See Remarks, page 5, last paragraph to page 6, first paragraph).

As set forth in this Office Action, Xu's reference provide one ordinary skill in the art the suggestion and motivation to use the method to detect the presence of DHA by binding to BLBP target protein. Ulman et al. reference provide the advantage of using a second antibody recognition of the complex of BLBP-DHA to increase sensitivity and efficiency of the assay.

Adams et al. reference

Applicant argues that Adam et al. reference using KOH to remove fatty acid from complex lipids is described in "a method for assessing the ability of a compound to alter arachidonate content of cellular phospholipids." Therefore, one would not be motivated to use a step of the aforementioned method in the binding affinity study of Xu et al., and even if they did so, one would not have a reasonable expectation of success.

Applicant's arguments have been considered but are not persuasive.

Again, Xu's reference has been shown to motivate one ordinary skill in the field to detect biological samples containing DHA in this Office Action. The DHA is a fatty acid in the form of lipid complex. One ordinary skill in the art would have used compound, such as KOH, an effective agent as taught by Adams et al. to remove and isolate DHA from the lipid complex if the *target molecule is DHA*, not other molecules (emphasis added).

Conclusion

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

March 24, 2005

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
11/10/05